REMARKS

Status Summary

Claims 29-38 are pending and were examined. The request for reconsideration, filed April 12, 2003, was entered. The rejections based on prior art have been withdrawn. Specifically, the examiner has withdrawn the rejection of claims 29-38 under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,312,694 to Thorpe et al. (Thorpe); the rejection of claims 29 and 34 under 35 U.S.C. § 102(b) as allegedly anticipated by Vogt et al. (1997) *Am. J. Obstet. Gynecol.* 177:964-972 (Vogt); the rejection of claims 29 and 34 under 35 U.S.C. § 102(b) as allegedly anticipated by Umeda et al. (1989) *J. of Immunol.* 143:2273-2279 (Umeda); the rejection of claims 29 and 34 under 35 U.S.C. § 102(b) as allegedly anticipated by Rote et al. (1993) *Clin. Immunol. And Immunopathogy* 66:193-200 (1993) (Rote); and the rejection of claims 29-38 under 35 U.S.C. § 103(a) as allegedly unpatentable over Rote or Umeda or Vogt in view of Thorpe.

Claims 29-38 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking adequate written description of the invention. Claims 29-38 are also rejected under § 112, first paragraph, as allegedly failing to enable practice of the invention.

Claim 1 is amended as indicated above. Claims 30-31 and 35-36 are canceled. Reconsideration in view of the amendments and following remarks is respectfully requested.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 29-38 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking adequate written description of the invention. Specifically, the examiner contends that the mammalian genome can encode antibodies having 10^6-10^{10} different variable regions, and that the specification does not describe which antibodies, other than 2E7, would be able to bind phosphatidyl serine. The examiner also contends that the specification does not teach human antibodies having the claimed properties. Official Action, pages 3-4, item 11. This rejection is respectfully traversed.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement (herein after the "Guidelines") teach that "[t]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." 66 Fed. Reg. 1099, 1104 (2001).

Possession of the invention can be shown in any one of several ways, including by a description of physical properties in combination with a description of functional characteristics. *Id.* at 1106.

Each of claims 29-38 refers to an antibody in terms of its physical properties, *i.e.*, having the light chain variable region of an antibody that recognizes e-aminocaprioic acid, and the heavy chain variable region of an antibody that recognizes p-azaphenylarsanate.

With respect to the examiner's argument the specification does not describe which antibodies, among the 10^6-10^{10} different antibodies encoded by the mammalian genome, applicant responds that the disclosure of the amino acid sequence of the 2E7 antibody completely describes antibodies of the invention. Specifically, claims 29-38 are directed to antibodies having light chain variable region of an antibody that recognizes e-aminocaprioic acid, and the heavy chain variable region of an antibody that recognizes p-azaphenylarsanate. The existence of a diverse repertoire of antibody molecules is not relevant to a description of the presently claimed antibodies.

The 2E7 antibody, which has the above-noted light and heavy chain variable regions, specifically binds to phosphatidyl serine (*see* Figure 1 of the application). Naturally occurring antibodies are tetrameric (H_2L_2) glycoproteins composed of two identical light (L) chains and two identical heavy (H) chains. Each of the light and heavy chains is characterized by an amino-terminal variable region and a constant region. The variable regions of each of light and heavy chain align to form the antigen-binding domain. The variable domains differ extensively in sequence among antibodies, which accounts for their diversity of antigen specificities. *See* Janeway, Jr. CA, et al. (2001) Immunobiolgy: the immune system in health and disease, Garland Publishing, New York, p. 96 (copy enclosed). Thus, antibodies having the disclosed 2E7 light and heavy chain variable regions include the 2E7 antigen-binding site, which binds to phosphatidyl serine.

The specification also discloses functional properties of an anti-PS antibody of the invention, including an ability to mediate complement dependent cytolysis (CDC), an ability to mediate macrophage phagocytosis, and an ability to inhibit tumor growth. Techniques for determining the claimed functional properties are described in the application as originally filed, including, for example, at page 31, line 12, through page 32, line 15 (CDC); page 32, line 17, through page 34, line 3 (phagocytosis); and page 35, line 8, through page 36, line 3 (tumor growth delay).

None of claims 29-38 refer to an anti-PS antibody based solely on functional description. In accordance with the Guidelines, claims 29-38 include a functional description in addition to a description of the physical properties of an anti-PS antibody. Specifically, claim 29 identifies an antibody of the invention as having an ability to mediate complement dependent cytotoxicity against a human tumor cell that expresses phosphotidyl serine. Claims 30-38 ultimately depend from claim 29 and thus also include this element.

Following a review of the disclosure of the instant application, a skilled artisan would readily understand that the applicant was in possession of anti-PS antibodies having the specified variable regions and an ability to mediate complement dependent cytotoxicity.

Based on the foregoing arguments, the instant application is believed to fully describe the invention of claims 29, 32-34, and 37-38 in accordance with the requirements of § 112, first paragraph. Claims 30-31 and 35-36 are canceled, and the rejection these claims is thereby rendered moot. Thus, applicant respectfully requests withdrawal of the rejection of claims 28-39 based on perceived lack of adequate description.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph -- Enablement

Claims 29-38 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to enable practice of the invention. Specifically, the examiner contends that the specification is does not enable preparation of any antibody that binds phosphatidyl serine wherein the light chain variable region is also present in an antibody that binds e-aminocaprioic acid and wherein the heavy chain variable region is also present in an antibody that binds p-azaphenylarsanate, including a human antibody. Official Action, pages 4-7, item 12. This rejection is respectfully traversed.

Claim 1 is amended to specify antibodies having light chain and heavy chain variable regions of the 2E7 antibody, which includes the 2E7 antibody as well as chimeric and humanized antibodies that contain the 2E7 variable regions. The examiner states that the specification is enabling for the 2E7 antibody and humanized and chimeric antibodies when proper deposit requirements are met. Thus, this rejection is believed to be rendered substantially moot by the present amendment.

With respect to the examiner's requirement that the 2E7 antibody be deposited, applicant responds that the claimed antibodies can be readily prepared based on the availability of the sequences of the light chain and heavy chain variable region sequences. As

noted in the application at page 34, the light chain variable region sequence is described in Elliot et al. (1984) *J Immunol* 133:2757-61, and the heavy chain variable region sequence is described in Gefter et al. (1984) *Ann Immunol* (Paris) 135C(1):17-30. Numerous techniques for preparing chimeric and humanized antibodies based on knowledge of the variable region sequences. *See e.g.*, Morrison et al. (1984) *Proc Natl Acad Sci USA* 81:6851-55; Morrison et al. (1988) *Adv Immunol* 44:65-92; Verhoeyen et al. (1988) *Science* 239:1534-36; Padlan (1991) *Molec Immunol* 28:489-98; and Padlan (1994) *Molec Immunol* 31:169-217 (incorporated by reference on pages 13-14 of the instant application). Thus, a skilled artisan can prepare the antibodies of claims 29, 32-34, and 37-38 in the absence of undue influence.

Based on the foregoing, applicant respectfully requests withdrawal of the rejection of claims 29, 32-34, and 37-38 under § 112, first paragraph as allegedly non-enabling. Claims 30-31 and 35-36 are canceled, and thus the rejection with respect to these claims is rendered moot.

Conclusion

The rejections under 35 U.S.C. § 112 having been addressed, it is respectfully submitted that the present application is in condition for allowance. If any points remain in issue, which the examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,
PILLSBURY WINTHROP LLP

Thomas A. Cawley, Jr., Ph.D.
Registration No. 40,944

P.O. Box 10500
McLean, VA 22102
(703) 905-2144 Direct Dial
(703) 905-2500 Facsimile

Date: October 16, 2003

TAC/JBM:ntb